

Prescribing Information as of December 1997

LOPROX®
(ciclopirox) **SPECIMEN**
Cream 0.77%

FOR DERMATOLOGIC USE ONLY.
NOT FOR USE IN EYES. 50016050

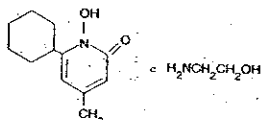
DESCRIPTION

LOPROX® (ciclopirox) Cream 0.77% is for topical use.

Each gram of LOPROX Cream contains 7.70 mg of ciclopirox (as ciclopirox olamine) in a water miscible vanishing cream base consisting of purified water USP, octyldodecanol NF, mineral oil USP, stearyl alcohol NF, cetyl alcohol NF, cocamide DEA, polysorbate 60 NF, myristyl alcohol NF, sorbitan monostearate NF, lactic acid USP, and benzyl alcohol NF (1%) as preservative.

LOPROX Cream contains a synthetic, broad-spectrum, antifungal agent ciclopirox (as ciclopirox olamine). The chemical name is 6-cyclohexyl-1-hydroxy-4-methyl-2(1H)-pyridone, 2-aminoethanol salt.

The CAS Registry Number is 41621-49-2. The chemical structure is:



LOPROX Cream has a pH of 7.

CLINICAL PHARMACOLOGY

Ciclopirox is a broad-spectrum, antifungal agent that inhibits the growth of pathogenic dermatophytes, yeasts, and *Malassezia furfur*. Ciclopirox exhibits fungicidal activity *in vitro* against isolates of *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, *Microsporum canis*, and *Candida albicans*.

Pharmacokinetic studies in men with tagged ciclopirox solution in polyethylene glycol 400 showed an average of 1.3% absorption of the dose when it was applied topically to 750 cm² on the back followed by occlusion for 6 hours. The biological half-life was 1.7 hours and excretion occurred via the kidney. Two days after application only 0.01% of the dose applied could be found in the urine. Fecal excretion was negligible.

Penetration studies in human cadaverous skin from the back, with LOPROX (ciclopirox) Cream with tagged ciclopirox showed the presence of 0.8 to 1.6% of the dose in the stratum corneum 1.5 to 6 hours after application. The levels in the dermis were still 10 to 15 times above the minimum inhibitory concentrations.

Autoradiographic studies with human cadaverous skin showed that ciclopirox penetrates into the hair and through the epidermis and hair follicles into the sebaceous glands and dermis, while a portion of the drug remains in the stratum corneum.

Draize Human Sensitization Assay, 21-Day Cumulative Irritancy study, Phototoxicity study, and Photo-Draize study conducted in a

total of 142 healthy male subjects showed no contact sensitization of the delayed hypersensitivity type, no irritation, no phototoxicity, and no photo-contact sensitization due to LOPROX Cream.

INDICATIONS AND USAGE

LOPROX Cream is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*; candidiasis (moniliasis) due to *Candida albicans*; and tinea (pityriasis) versicolor due to *Malassezia furfur*.

CONTRAINDICATIONS

LOPROX Cream is contraindicated in individuals who have shown hypersensitivity to any of its components.

WARNINGS

General

LOPROX (ciclopirox) Cream is not for ophthalmic use.

PRECAUTIONS

If a reaction suggesting sensitivity or chemical irritation should occur with the use of LOPROX Cream, treatment should be discontinued and appropriate therapy instituted.

Information for Patients

The patient should be told to:

1. Use the medication for the full treatment time even though symptoms may have

improved and notify the physician if there is no improvement after four weeks.

2. Inform the physician if the area of application shows signs of increased irritation (redness, itching, burning, blistering, swelling, oozing) indicative of possible sensitization.

3. Avoid the use of occlusive wrappings or dressings.

Carcinogenesis, Mutagenesis, Impairment of Fertility

A carcinogenicity study in female mice dosed cutaneously twice per week for 50 weeks followed by a 6-month drug-free observation period prior to necropsy revealed no evidence of tumors at the application site.

The following *in vitro* and *in vivo* genotoxicity tests have been conducted with ciclopirox olamine: studies to evaluate gene mutation in the Ames *Salmonella*/Mammalian Microsome Assay (negative) and Yeast Saccharomyces *Cerevisiae* Assay (negative) and studies to evaluate chromosome aberrations *in vivo* in the Mouse Dominant Lethal Assay and in the Mouse Micronucleus Assay at 500 mg/kg (negative).

The following battery of *in vitro* genotoxicity tests were conducted with ciclopirox: a chromosome aberration assay in V79 Chinese Hamster Cells, with and without metabolic activation (positive); a gene mutation assay in the HGPRT - test with V79 Chinese Hamster Cells (negative); and a primary DNA damage assay (i.e., unscheduled DNA Synthesis Assay in A549 Human Cells (negative)). An *in*

vitro Cell Transformation Assay in BALB/C3T3 Cells was negative for cell transformation. In an *in vivo* Chinese Hamster Bone Marrow Cytogenetic Assay, ciclopirox was negative for chromosome aberrations at 5000 mg/kg.

Pregnancy Category B

Reproduction studies have been performed in the mouse, rat, rabbit, and monkey, (via various routes of administration) at doses 10 times or more the topical human dose and have revealed no significant evidence of impaired fertility or harm to the fetus due to ciclopirox. There are, however, no adequate or well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when LOPROX (ciclopirox) Cream is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients below the age of 10 years have not been established.

ADVERSE REACTIONS

In all controlled clinical studies with 514 patients using LOPROX Cream and in 296 patients using the vehicle cream, the incidence of adverse reactions was low. This included pruritus at the site of application in one patient and worsening of the clinical

signs and symptoms in another patient using ciclopirox cream and burning in one patient and worsening of the clinical signs and symptoms in another patient using the vehicle cream.

DOSAGE AND ADMINISTRATION

Gently massage LOPROX (ciclopirox) Cream 0.77% into the affected and surrounding skin areas twice daily, in the morning and evening. Clinical improvement with relief of pruritus and other symptoms usually occurs within the first week of treatment. If a patient shows no clinical improvement after four weeks of treatment with LOPROX Cream, the diagnosis should be redetermined. Patients with tinea versicolor usually exhibit clinical and mycological clearing after two weeks of treatment.

HOW SUPPLIED

LOPROX Cream is supplied in 15 gram (NDC 0039-0190-15), 30 gram (NDC 0039-0190-30), and 90 gram (NDC 0039-0190-90) tubes.

Store between 59 and 86°F (15 and 30°C).

LoProx REG TM HOECHST AG

Prescribing Information as of December 1997



Hoechst-Roussel Pharmaceuticals
Division of Hoechst Marion Roussel, Inc.
Kansas City, MO 64137

REG TM Made in Germany

50016050

NDC 0039-0190-15



Loprox®
(ciclopirox)

15 g

CREAM 0.77%

SPECIMEN

**FOR DERMATOLOGIC USE ONLY.
NOT FOR USE IN EYES.**

Rx ONLY

Keep this and all medication out of the reach of children.
Store between 59 and 86 °F (15 and 30 °C).

Usual Dosage: Gently massage into the affected and
surrounding skin areas twice daily, in the morning and evening.
See insert for full prescribing information.

Each gram contains: 7.70 mg ciclopirox (as ciclopirox olamine)
in a water miscible vanishing cream base consisting
of purified water USP, octyldodecanol NF, mineral oil USP,
stearyl alcohol NF, cetyl alcohol NF, cocamide DEA,
polysorbate 60 NF, myristyl alcohol NF, sorbitan monostearate
NF, lactic acid USP, and benzyl alcohol NF (1%) as preservative.
Lot No. - Exp. Date, see crimp.

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Manufactured by:

Loprox REG TM HOECHST AG

HOECHST MARION ROUSSEL Pharmaceuticals
Division of Hoechst Marion Roussel, Inc.
Kansas City, MO 64627
Hoechst Marion Roussel AG

Made in Germany

50016496

126536 B



LOT:

EXP:



NDC 0039-0190-15
Loprox[®]
(ciclopirox)
CREAM 0.77%

15 g



3 0039-0190-15 3

NDC 0039-0190-15
Loprox[®]
(ciclopirox)
CREAM 0.77%
15 g



Directions for puncturing tube seal:
Remove cap. Turn cap upside down and place puncture tip onto tube. Push cap until tube end is punctured.
Screw cap back on to reseal tube.
Use the cap to massage cream into the affected and surrounding skin areas twice daily, in the morning and evening.
See package insert for full prescribing information.
Each gram contains: 770 mg ciclopirox (as ciclopirox olamine) in a water-soluble, soothing cream base consisting of purified water USP, octyldodecanol NF, mineral oil USP, stearic acid NF, cetyl alcohol NF, cocamide DEA, polysorbate 60 NF, myristyl alcohol NF, sorbitan monostearate NF, lactic acid USP, and benzyl alcohol NF (1%) as preservative.
Store between 59 and 86°F (15 and 30°C). Keep this and all medication out of the reach of children.
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123456 800
1234567890

NDC 0039-0190-15
Loprox[®]
(ciclopirox)
CREAM 0.77%
FOR DERMATOLOGIC USE ONLY. NOT FOR USE IN EYES.
Rx ONLY

15 g

SPECIMEN

Loprox REG TM HOECHST AG
NSN 6505-01-189-3948

Manufactured by:
HOECHST-ROUSSEL Pharmaceuticals
Division of Hoechst Marion Roussel, Inc.
Kansas City, MO 64137
Made in Germany

REG TM HOECHST AG

126527 B

50016500

NDC 0039-0190-30

30 g



Loprox[®]
(ciclopirox)

CREAM 0.77 %

FOR DERMATOLOGIC USE ONLY.
NOT FOR USE IN EYES.

Rx ONLY

Keep this and all medication out of the reach of children.
Store between 59 and 86 °F (15 and 30 °C).

Usual Dosage: Gently massage into the affected and
surrounding skin areas twice daily, in the morning and evening.
See insert for full prescribing information.

Each gram contains: 7.70 mg ciclopirox (as ciclopirox olamine)
in a water miscible vanishing cream base consisting
of purified water USP, octyldodecanol NF, mineral oil USP,
stearyl alcohol NF, cetyl alcohol NF, cocamide DEA,
polysorbate 60 NF, myristyl alcohol NF, sorbitan monostearate
NF, lactic acid USP, and benzyl alcohol NF (1%) as preservative.

Lot No. - Exp. Date, see crimp.

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Made in Germany

Loprox REG TM HOECHST AG

Manufactured by:



HOECHST-ROUSSEL Pharmaceuticals
Division of Hoechst Marion Roussel, Inc.
Kansas City, MO 64137

REG TM HOECHST AG



50016497
126557 B

NDC 0039-0190-30

Loprox[®]
(ciclopirox)

CREAM 0.77%

Directions for puncturing tube seal:

Remove cap. Turn cap upside down and place puncture tip onto tube. Push cap until tube end is punctured. Screw cap back on to reseal tube.

Usual Dosage: Gently massage into the affected and surrounding skin areas twice daily, in the morning and evening. See insert for full prescribing information.

Each gram contains: 7.70 mg ciclopirox (as ciclopirox clamine) in a water miscible vanishing cream base consisting of purified water USP, octyldodecanol NF, mineral oil USP, stearyl alcohol NF, cetyl alcohol NF, cocamide DEA, polysorbate 80 NF, myristyl alcohol NF, sorbitan monooleate NF, lactic acid USP, and benzyl alcohol NF (1%) as preservative.

Store between 59 and 86°F (15 and 30°C). Keep this and all medication out of the reach of children.

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1234 87890
234567890

30 g



3 0039-0190-30 6

NDC 0039-0190-30
Loprox[®]
(ciclopirox)
CREAM 0.77%
30 g

NDC 0039-0190-30

Loprox[®]
(ciclopirox)

CREAM 0.77%

FOR DERMATOLOGIC USE ONLY. NOT FOR USE IN EYES.
Rx ONLY

SPECIMEN

30 g

Loprox REG TM HOECHST AG
NSN 6505-01-180-6961

Manufactured by:
HOECHST-ROUSSEL Pharmaceuticals
Division of Hoechst Marion Roussel, Inc.
Kansas City, MO 64137
Made in Germany

REG TM HOECHST AG

126533 B

50016493

NDC 0039-0190-90

90 g



Loprox[®]
(ciclopirox)

SPECIMEN

CREAM 0.77%

**FOR DERMATOLOGIC USE ONLY.
NOT FOR USE IN EYES.**

Rx ONLY

Keep this and all medication out of the reach of children.
Store between 59 and 86°F (15 and 30°C).

Usual Dosage: Gently massage into the affected and surrounding skin areas twice daily, in the morning and evening. See insert for full prescribing information.

Each gram contains: 7.70 mg ciclopirox (as ciclopirox olamine) in a water miscible vanishing cream base consisting of purified water USP, octyldodecanol NF, mineral oil USP, stearyl alcohol NF, cetyl alcohol NF, cocamide DEA, polysorbate 60 NF, myristyl alcohol NF, sorbitan monostearate NF, lactic acid USP, and benzyl alcohol NF (1%) as preservative.

Lot No. - Exp. Date, see crimp.

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Loprox REG TM HOECHST AG

Manufactured by:



HOECHST-ROUSSEL Pharmaceuticals
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Kansas City, MO 64137

REG TM HOECHST AG



50016498
126537 B



LOT:

EXP:



Loprox[®]

(ciclopirox)

90 g

CREAM 0.77 %

**FOR DERMATOLOGIC USE ONLY. NOT FOR USE IN EYES.
Rx ONLY**

3 0039-0190-90 0



NDC 0039-0190-90
Loprox[®]
(ciclopirox)
CREAM 0.77 %
90 g



Directions for puncturing tube seal:
Remove cap. Turn cap upside down and place puncture tip onto tube. Push cap until tube end is punctured. Screw cap back on to reseal tube.

Usual Dosage: Gently massage into the affected and surrounding skin areas twice daily, in the morning and evening. See insert for full prescribing information.

Each gram contains: 7.70 mg ciclopirox (as ciclopirox olamine) in a water miscible vanishing cream base consisting of purified water USP, octyldodecanol NF, mineral oil USP, stearyl alcohol NF, cetyl alcohol NF, cocamide DEA, polysorbate 60 NF, myristyl alcohol NF, sorbitan monostearate NF, lactic acid USP, and benzyl alcohol NF (1%) as preservative.

Store between 59 and 86°F (15 and 30°C). Keep this and all medication out of the reach of children.
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22457220
1234567890



Loprox[®]

(ciclopirox)

SPECIMEN

NDC 0039-0190-90

90 g

CREAM 0.77 %

**FOR DERMATOLOGIC USE ONLY. NOT FOR USE IN EYES.
Rx ONLY**

126546 B

Manufactured by:
HOECHST-ROUSSEL Pharmaceuticals
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REG TM HOECHST AG

50016494